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(54) Title: ISCOM OR ISCOM-MATRIX COMPRISING A MUCUS TARGETTING SUBSTANCE AND OPTIONALLY, AN ANTIGEN

(57) Abstract

The invention relates to immunogenic complex comprising iscom and/or iscommatrix and mucus targetting molecules for use for preparing vaccines and immune stimulating compositions for oral, nasal, urogenital and/or rectal administration. The immunogenic complex may comprise at least one glycoside and at least one lipid and a) at least one mucus targetting molecule chosen among substances that target lymphatic tissue and induce immune response when administrated locally on mucous membranes; and b) possibly also one passenger antigen chosen among pharmacologically immune active or immune substances that do not easily reach lymphatic tissue through mucous membranes.

parts are not dissolvable. The solubilising agent can be removed, for example, by gel filtration, ultrafiltration, dialysis or electrofores. The matrices may then be purified from an excess of sterol and saponin by means of, for example, centrifugation through a density gradient or by gel centrifigation.

The solubilising agent may be any of those mentioned in EP 0 436 629 B1, p. 5, lines 24-45. The other components and the preparation process are also described in this document.

Passenger and mucus targeting molecule can be bound to the matrices using current binding-conjugation methods, see above. It is also feasible to mix adjuvant molecules and/or passenger antigens with an iscom molecule in which the passenger antigen or the adjuvant molecule has been integrated, or with iscom and/or matrix complexes to which the passenger antigen or the mucus targeting molecule has been connected. It is also possible to mix both mucus targeting molecule and passenger antigen with an iscom complex or matrix in a separate entity, in which case the iscom complex contains a different antigen molecule.

The glycosides used in the preparation may be those described in EP 0 109 942 B1, p. 4, last paragraph. The preferred method is to use saponins such as triterpensaponins, particularly Quil A or defined components of it, particularly those described in the applicant's European patent EP 0 436 620 B1 p. 4 lines 19-46. These may be QHA, QHB, QHC or other compositions of Quil A, such as 703. Glycosides are adjuvants. Or such components described by Kensil, Kersten or Dalsgaard (Kensil, C.R., Patel, U., Lennick, M. and Marciani, D., J. Immunol, 146, 431-437, 1991; Kersten, G.G.A., Spiekstra, A., Beuvery, E.C. and Commelin, D.J.A. BBA1062, 165-171, 1991; or patent WO95/09179 Dalsgaard). It is also possible to incorporate other adjuvants or immune-modulating components than the glycosides in the iscoms or in the matrices as mentioned in EP 0 436 620 B1.

on pp. 4-8. The preferred procedure is to put in the additive before adding the lipids and glycosides.

Furthermore, you can use a base consisting of mucus targeting molecules or passenger antigens that are more or less purified, synthetisized chemically or prepared using a hybrid-DNA technique according to EP 0 109 942 B1 as on pp. 4-8. In this case it is appropriate to add the lipids before the complex has been isolated and cleaned, as is described in the applicant's European patent EP 0 242 380 B1.

The lipids used are particularly the kind described in the applicant's patent EP 0 109 942 B1 in particular on p. 3 and in EP 0 436 620 B1, p. 7, lines 7-24. Sterols such as cholesterol and phospholipids such as phosphatidylethanolamine and phosphatidylcholine GM1, were particularly used.

The lipids may also include lipid-containing substances that bind to cell-forming components, for instance glycolipids such as the receptor of cholera toxin, the gangliosid GM1, and fucosed blood group antigen. The cell-binding components can then function as mucus targeting molecules and be tied to the lipid-containing substances by simply mixing with complexes that contain them.

It is also possible to first prepare iscom particles from a mucus targeting or passenger antigen and then add on the passenger and mucus targeting antigens respectively using current conjugation methods, preferably chemical coupling methods, as is described in the applicant's European patents EP 0 180 564 B1 and EP 0 436 620 B1.

The base could also be matrices that are prepared by solubilising at least one sterol in a solubilising agent, adding the glycoside or the saponins and the other lipids, after which the solution agent may be removed if desired, i e if it cannot be accepted in the final product. Matrices are usually transferred to a water solution in which the individual